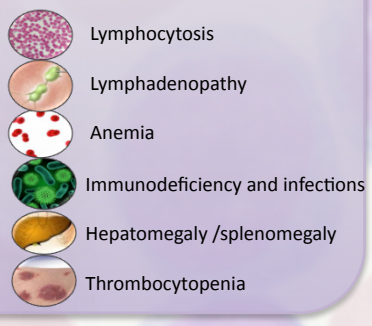
GENETIC ABNORMALITIES IN CHRONIC LINPHOCITIC LEUKEMIA AND THEIR PROGNOSTIC VALUE

Author: Leticia Suárez Cabrera | Degree: Genetics | Universidad Autónoma de Barcelona

INTRODUCTION

Chronic Linphocitic Leukemia is the most common type of leukemia in adults. It represents 25 to 35 % of all kinds of leukemia and affects more men than women. It is characterized by accumulation of mature B cells in blood, secondary lymphoid organs and bone marrow. It is a very heterogeneous disease, with a wide clinical development, from nearly asymptomatic with slow progressive expansion, to very aggressive, with quick evolution of the disease and an average survival of one or two years.

Its main features are:



- Lymphocytosis
- Lymphadenopathy
- Anemia
- Immunodeficiency and infections
- Hepatomegaly /splenomegaly
- Thrombocytopenia

OBJECTIVES

The aim of this work is to carry out a bibliographic review about the most frequent genetic abnormalities in CLL and their usefulness to perform and accurate prognosis, which will help to classify patients in different risk subgroups so they can be treated with the best therapy available.

MATERIAL AND METHODS

It is a bibliographic review, so the information and images were mostly obtained from articles, reviews, books and doctoral thesis related with the topic, all of them cited in the reference section.

GENETIC AND CITOGENETYCS OF CLL AND THEIR PROGNOSIS VALUE

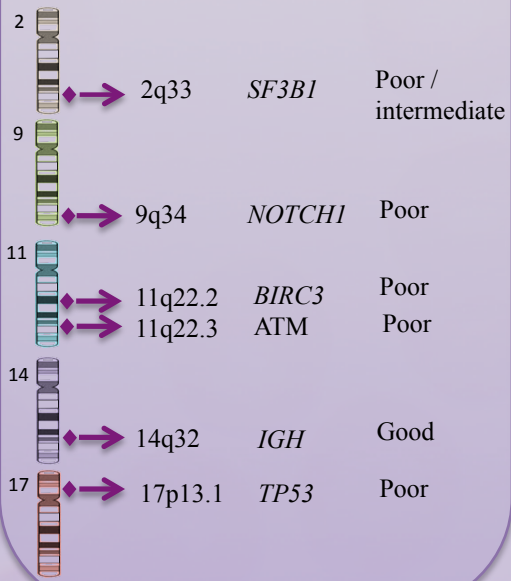
CYTOGENETIC ABERRATIONS AND THEIR PROGNOSTIC VALUE

Chromosomal aberrations are detected in over 80% of patients analysed. In order to classify each patient depending on the alteration they carry, a hierarchical model, based in five categories, was designed, correlating the abnormalities detected by FISH and the course of the disease.

	Prevalence	Prognosis and average survival	Related abnormalities
17p13 deletion	7%	Poor 32 months	Mutation of *TP53*
11q22-q23 deletion	18%	Poor 79 months	Mutation of *ATM*
12 trisomy	16%	Intermediate 114 months	Gene dosage effect
13q14 deletion	55%	Good 133 months	Mutation of miR15 and miR16
Normal karyotype	18%	Intermediate 111 months	None

GENETIC MUTATIONS AND THEIR PROGNOSTIC VALUE

Cytogenetic analysis is not enough to make a complete prognosis of the disease. The discovery of new alterations, such as recurrent gene mutations, are helping to identify new potential biomarkers with important prognostic value.



DISCUSION

CLL is characterised by a set of well defined recurrent alterations, which seem to have valuable clinical importance, in some cases better established than others, like TP53 alteration, which at the present is the only molecular biomarker that changes therapeutic approaches. That said, novel lesions in genes such as *SF3B1, NOTHC1 or BIRC3* might also have informative prognosis value and help to make decisions about treatment in future. From a clinical perspective, attempts to develop a new prognostic model which would include both, chromosomal abnormalities and gene mutations, have already begun, but some discrepancies are emerging from different studies, therefore, additional examinations must be warranted before these schemes can be applicable.

BIBLIOGRAPHY

1. Sutton, L. and Rosenquist, R. **Deciphering the molecular landscape in chronic lymphocytic leukemia: time frame of disease evolution**. Haematologica, 100(1), p.7-16 (2015)
2. Foa, R., Del Giudice, I., Guarini, A., Rossi, D. and Gaidano, G. **Clinical implications of the molecular genetics of chronic lymphocytic leukemia**. Haematologica, 98(5), p.675-685 (2013)
3. Puiggros, A., Blanco, G. and Espinet, B. **Genetic Abnormalities in Chronic Lymphocytic Leukemia: Where We Are and Where We Go**. BioMed Research International, p.1-13 (2014).
4. Wang, C. and Wang, X. **The role of TP53 network in the pathogenesis of chronic lymphocytic leukemia**. Int J Clin Exp Pathol, 6(7), p.1223-9 (2013).

UAB